The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JAGDISH PARASRAMPURIA,
MAXINE B. YONKER,
KENNETH E. SCHWARTZ and
MARC J. GURWITH

Appeal No. 2005-2027
Application No. 09/526,802

ON BRIEF

Before ELLIS, ADAMS and GRIMES, Administrative Patent Judges.

ELLIS, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal pursuant to 35 U.S.C. § 134 from the examiner's final rejection of claims 1-10 and 36-39, the only claims remaining. Claims 11-35 have been cancelled.

Claims 1, 5, 36 and 38 are representative of the subject matter on appeal and read as follows:

Claim 1. A pharmaceutical formulation comprising dehydroepiandrosterone (DHEA), at least 85% of which is present as the form I polymorph, and at least one pharmaceutical excipient.

Claim 5. A method for preparing a solid DHEA formulation, said method comprising: mixing at least one solid pharmaceutical excipient with dehydroepiandrosterone (DHEA), at least 85% of which is present as the form I polymorph.

Claim 36. A pharmaceutical formulation comprising dehydroepiandrosterone (DHEA), at least 85% of which is present as the form I polymorph as determinable by solid state 13C NMR spectroscopy, and at least one pharmaceutical excipient.

Claim 38. A method for preparing a solid DHEA formulation, said method comprising: mixing at least one solid pharmaceutical excipient with dehydroepiandrosterone (DHEA), at least 85% of which is present as the form I polymorph as determinable by solid state 13C NMR spectroscopy.

The references relied upon by the examiner are:

Morales et al. (Morales)	5,407,927	Apr. 18, 1995
Loria et al. (Loria)	5,077,284	Dec. 31, 1991

Chang et al. (Chang), "Solid State Characterization of Dehydroepiandrosterone," J. Pharm. Sci., vol. 84(10), pp. 1169-79 (October 1995).

Claims 1-10 and 36-39 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Morales, Loria and Chang.

We reverse.

Background and Discussion

As indicated by the claims above, the present invention is directed to compositions and methods of formulating DHEA, a naturally occurring intermediate formed in vivo during the course of synthesis of steroids from cholesterol. Specification,

p. 2, lines 10-12. DHEA, as a pharmaceutical formulation, has been proposed for use in treating systemic lupus erythematosus, primary adrenal insufficiency, Addison's disease, reduced libido, obesity, osteoporosis and fibromyalgia. Id., lines 17-21. Commercially available DHEA compositions, however, contain random concentrations of polymorphic forms that can hinder DHEA bioavailability. Id., p. 3, lines 3-13. The appellants' invention is enriched for polymorph form I, which is said to increase the bioavailability and efficacy of DHEA. Id., lines 14-16.

The examiner asserts that Chang discloses polymorphic forms of DHEA (forms I-III), solid-state crystallization of these forms, and that, of all of these forms, form I is the most stable.[1] Answer, p. 4. The examiner points out that Chang teaches the estimation of purity of polymorphic forms I-III through analysis of X-ray powder diffraction patterns. Id., pp. 4-5.

According to the examiner, because Chang discloses that the purity of their form I DHEA preparations "are as high as 95%[,]"

> . . . [i]t would have been obvious to one skilled in the art at the time when instant invention was made, to be motivated to prepare additional beneficial preparations and formulations of DHEA[.] [T]he preparation may contain at least 95% of DHEA and expected to contain especially polymorph form I because this is the most stable form.
> * * *

[1] The examiner argues that Morales and Loria disclose the formulation of DHEA for the treatment of various diseases. Id., p. 5. Presumably, the examiner recites these teachings to satisfy the limitations in the claims with respect to pharmaceutical formulations. However, she makes no arguments in that regard. The examiner's oversight is of little consequence because all the claims require that at least 85% or more of the DHEA in the formulations must be present as the form I polymorph. Since we find that the examiner has not sustained her burden of establishing that the claimed amount of DHEA form I would have been obvious to one of ordinary skill in the art, we need not consider the teachings of Morales and Loria in our deliberations.

> C13 NMR in claims for polymorphic form has been considered, but . . . th[e] prior art compound contains polymorph I[.] [T]herefore, in composition and formulation[,] this will not [be] patentab[ly] distinct.
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> It had been held that by changing the form, purity or other characteristics of an old product does not render the novel form patentable where the difference in form, purity or characteristic was inherent in or rendered obvious by the prior art. In re Cofer, 53 CCPA (1966) 830, 835, 354 F[.]2d 664, 668, 148 USPQ 268, 271.
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> . . . [T]he Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Id., pp. 5-6.

The appellants, on the other hand, point to the specification which teaches that Chang's method for producing form I DHEA results in form I preparations that are actually contaminated with a previously uncharacterized contaminant, form VI. Appeal Brief, p. 5. The appellants assert that Chang's incorrect assumptions of form I purity stemmed from the fact that Chang did not employ ^{13}C-solid state NMR (^{13}C-SSNMR) analysis, the only analytical method known to distinguish form I from form VI. Id., p. 5. Additionally, the appellants contend that in order to prepare "truly pure form I,"

> . . . [a]ppellants crystallized DHEA from 2-propanol, acetone, or acetonitrile, as described by Chang, and then carried out an additional step. Specifically, this step entailed 'suspending the precipitate from the first step in ethyl acetate (about 100 mL/30g of DHEA) and stirring the resulting slurry at room temperature for about one week, followed by filtration.' Appellants confirmed the purity of this preparation by ^{13}C-SSNMR analysis . . . .

Id.

Finally, the appellants contend that X-ray powder diffraction patterns cannot be used to accurately measure DHEA purity, contrary to the teachings of Chang. In

support of their contention, the appellants have submitted a Declaration of Dr. Patrick Stahly pursuant to 37 C.F.R. § 1.132. Through experimental data, Dr. Stahly demonstrates that: (1) Chang's method of DHEA crystallization can yield mixtures of form I DHEA with 30-40% form VI DHEA; (2) a mixture of form I and form VI DHEA exhibits the same X-ray powder diffraction pattern as a pure form I preparation; and (3) ^{13}C-SSNMR analysis of a form I:VI preparation and a pure form I preparation show that the mixture preparation only contains 60-70% form I DHEA. See Appeal Brief, p. 6.

It is well established that the examiner has the initial burden under 35 U.S.C. § 103 to establish a prima facie case. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); In re Piasecki, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984). To that end, it is the examiner's responsibility to show that some objective teaching or suggestion in the applied prior art, or knowledge generally available in the art, would have led one of ordinary skill in the art to combine the references to arrive at the claimed invention. Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 745 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

In the present case, we find that the examiner has not provided any reason(s) based on the applied prior art as to why the claimed invention would have been obvious to one of ordinary skill in the art. That is, if we look at the subject matter recited in claims 1, 5, 36 and 38, we find that each of these claims is directed to DHEA formulations, at least 85% of which is present as the form I polymorph. We agree with the examiner that Chang teaches that form I DHEA is the most stable polymorph and

that this form may ultimately lead to improved bioavailability (p. 1179); however, we do not find that Chang teaches or suggests DHEA formulations, at least 85% of which is present as the form I polymorph. To the contrary, although Chang discloses that "the purities of forms I-III and S1 are as high as 95%[,]" this reference also recognized that "X-ray diffraction patterns can potentially be employed as a method of estimating the purity of polymorphs of DHEA" [emphasis added]. Chang, p. 1175. Even Chang acknowledges the limitations of X-ray diffraction pattern (XRPD) analysis by noting that DHEA "forms S3 and S4 are indistinguishable in X-ray powder diffraction pattern [p. 1175]" because "similar XRPD patterns are obtained [p.1179]"; i.e., the XRPD peaks of forms S3 and S4 overlap. See Chang, Figure 6, p. 1176. Moreover, the appellants have provided substantive evidence in Dr. Stahly's declaration which the examiner has brushed aside. Contrary to the examiner's arguments, the appellants have demonstrated that none of Chang's analytical techniques could distinguish between form I and form VI DHEA and that Chang's preparations only contained 60-70% form I DHEA. Accordingly, it reasonably follows that we do not find Chang would have suggested to one of ordinary skill in the art a DHEA formulation at least 85% of which exists in the form I polymorph.

We also find the examiner's reliance on In re Cofer, 354 F.2d 664, 668, 148 USPQ 268, 271(C.C.P.A. 1966) to be misplaced in rejecting the appellants' claims which recite the limitation requiring the form I DHEA polymorph to be "determinable by solid state 13C NMR spectroscopy." See claims 36 and 38. According to the examiner,

"changing the form, purity or other characteristics of an old product does not render the novel form patentable where the difference in form, purity or characteristic was inherent in or rendered obvious by the prior art." Answer, p. 6. We disagree that Cofer stands for such a broad proposition. Rather, more accurately stated, the C.C.P.A. in that case found that the analysis of the patentability of a novel form should focus inter alia on " . . . whether the prior art suggests the particular structure or form of the compound or composition as well as suitable methods of obtaining that structure or form" [emphasis added]. Cofer, 354 F.2d at 668, 148 USPQ at 271. The mere fact that the prior art discloses the form I polymorph of DHEA does not render the claimed level of purity obvious.

Here, we agree with the appellants that because none of the cited references teaches or suggests that form VI DHEA is a substantial contaminant of form I DHEA preparations disclosed by Chang, there is, therefore, no motivation or suggestion to remove an unknown contaminant by any suitable method. Rather, on this record, the only suggestion we find of methods suitable for obtaining DHEA, at least 85% of which is present as the form I polymorph as determinable by solid state 13C NMR spectroscopy, is in the appellants' disclosure. Although Chang discloses the crystallization of form I DHEA by 2-propanol, acetone, or acetonitrile, the reference contains no teaching of the additional ethyl acetate purification step described in the appellants' specification. Thus, we find that the examiner has engaged in impermissible hindsight to arrive at the conclusion that the claimed invention would have been obvious

over Chang, Morales and Loria. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed. Cir. 1985); W.L. Gore & Assocs. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-313 (Fed. Cir. 1983) cert. denied 469 U.S. 851 (1984)("To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher").

In view of the foregoing, the decision of the examiner is reversed.

REVERSED

JOAN ELLIS
Administrative Patent Judge)

DONALD E. ADAMS
Administrative Patent Judge) BOARD OF PATENT APPEALS AND INTERFERENCES

ERIC GRIMES
Administrative Patent Judge)

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